PUBLIC SUMMARY DOCUMENT

Product: Ferric carboxymaltose, solution for I.V. use, 500mg in 10mL, Ferinject®
Sponsor: Vifor Pharma Pty Ltd
Date of PBAC Consideration: November 2013

1. Purpose of Application

The re-submission requested PBS listing as an unrestricted benefit for the treatment of iron deficiency anaemia.

2. Background

At the March 2013 meeting, the PBAC recommended listing ferric carboxymaltose (FCM) on the PBS as an unrestricted benefit for iron deficiency anaemia (IDA). Listing was recommended based on a cost-minimisation with intravenous (IV) iron polymaltose (IP). The equi-effective doses were based on a 1:1 ratio of iron delivered by those formulations.

The PBAC considered that there may be an advantage of FCM over IV IP in terms of reduced administration time but that this benefit had not been quantified and would need to be determined in order to justify a price advantage.

This re-submission is an attempt to address this issue.

The Public Summary Document from the March 2013 PBAC meeting is available on the PBS website.

3. Registration Status

Ferric carboxymaltose (FCM) was TGA registered on 21 April 2011 for the treatment of iron deficiency when oral iron preparations are ineffective or cannot be used. The diagnosis must be based on laboratory tests.

4. Listing Requested and PBAC's View

Consistent with the PBAC recommendation of the original submission (March 2013), the re-submission requested listing of FCM as an unrestricted benefit item on the PBS, for the treatment of iron deficiency anaemia. The listing request is for a single strength (500mg), for a maximum quantity of 2, with one repeat. This proposed listing differs from that requested in the original submission, which incorporated an Authority Required restriction and also included a 100mg vial size.

The PBAC noted that the Pre-PBAC Response stated that an Authority required listing is required to support any proposed risk sharing agreement. The PBAC did not consider that an Authority required listing was required in recommending listing and noted the Drug Utilisation Sub-Committee (DUSC) advice that a risk sharing agreement could be managed without an Authority required listing.

Further, the PBAC noted that the re-submission's decision to not request listing of a 100mg vial may lead to use beyond the requested listing for the 500mg vial with consequent additional cost to the Commonwealth.

5. Clinical Place for the Proposed Therapy

IDA is often a co-morbidity arising from a number of medical conditions, such as chronic kidney disease, inflammatory bowel disease, chronic heart failure, and women in the pregnant or postpartum period. Patients with IDA may have decreased functional ability, mental health or quality of life. In addition, IDA can amplify underlying chronic conditions thereby increasing the risk of hospitalisation and mortality.

Oral iron is the cornerstone for the treatment of IDA, however, it is known to take several months to be effective. Intravenous (IV) iron is considered when oral iron is not tolerated or is ineffective. IV iron will also be prescribed when a rapid increase in Hb level is clinically necessary to avoid physiological decompensation or blood transfusion (e.g. in patients with severe anaemia).

Ferric carboxymaltose is proposed as an alternative treatment to IV iron polymaltose (IP) for IDA patients who are intolerant or unresponsive to oral iron preparations and for patients who require rapid iron repletion.

6. Comparator

As in March 2013, the re-submission nominated IV IP as the main comparator. This was considered appropriate by the PBAC.

7. Clinical Trials

No head-to-head randomised controlled trials (RCTs) comparing FCM with IV IP were identified in the March 2013 submission. No additional trials were presented in the re-submission to those previously considered by the PBAC in March 2013.

Details of the trials have been previously reported in the March 2013 Public Summary Document.

8. Results of Trials

With regard to comparative effectiveness, the PBAC reiterated its previous consideration that although the clinical trials investigating FCM versus oral iron and IP versus oral iron were identified, no meaningful formal indirect comparison between the two trial sets could be performed.

No additional information with regard to comparative harms was provided in the re-submission.

9. Clinical Claim

The re-submission claimed that FCM is non-inferior in terms of comparative effectiveness and non-inferior in terms of comparative safety to IV IP.

The PBAC previously considered that the claim was not sufficiently supported by the evidence presented in the re-submission because of the lack of appropriate comparative trials of FCM and IV IP.

10. Economic Analysis

The re-submission presented a new cost analysis. The total pharmaceutical costs associated with FCM are higher than those for IP; however the re-submission claimed that patients will move to lower cost treatment settings reducing the average weighted treatment cost.

The PBAC agreed with the Economics Sub-committee (ESC) that the extent of shift to other treatment settings relied heavily on proportions of use drawn from survey data. Should these shifts not occur as predicted, the higher price for FCM would not be justified.

The PBAC noted that when the proportions of IP use in public hospitals as inpatients and outpatients were reversed (from that proposed in the re-submission), the proportion of FCM use in private hospital inpatients was higher than proposed in the re-submission,, the proportion of private hospital outpatient use was the same for both IP and FCM and the proportions of use in general practice remained the same as proposed in the re-submission, the difference in treatment costs resulted in a higher weighted treatment cost than that calculated in the re-submission. The PBAC noted that on the basis of this revised calculation, a price reduction would be required.

11. Estimated PBS Usage and Financial Implications

The likely number of patient episodes treated with FCM per year was estimated in the re-submission to be between 50,000 and 100,000 in Year 5, at an estimated net cost per year to the R/PBS of between $10 and $30 million in Year 5.

The PBAC agreed with the DUSC that FCM may facilitate greater use of iron infusions in specific settings where iron deficiency anaemia was a significant health issue and access to hospital-based care was extremely limited, in particular remote and regional areas. However, they also considered that the uptake and delivery of services by GPs would be highly variable across Australia and dependent on various factors such as activity based funding and resource utilisation in hospitals, fees for MBS services, and availability of equipment for infusion and monitoring.

The PBAC considered that the re-submission's approach to preparing the estimates was reasonable. The PBAC agreed with the DUSC that the treatment survey should be interpreted with caution due to external and internal validity concerns. In particular the PBAC agreed that the distribution of patients in non-admitted and admitted settings reported in the survey was highly variable and considered that the estimated proportions of people switching iron administration from hospital inpatient to hospital outpatient settings was inflated. The PBAC noted DUSC's advice that more clinics, employing nurses to deliver services such as FCM administration, may be set up in community settings in the future.

12. Recommendation and Reasons

The PBAC upheld its March 2013 recommendation to list ferric carboxymaltose on the PBS as an unrestricted benefit for iron deficiency anaemia (IDA), on a cost-minimisation basis

with IV iron polymaltose. The equi-effective doses should be based on a 1:1 ratio of iron delivered by those formulations.

The PBAC reiterated its view that there is a likely to be an advantage of FCM over IP given intravenously in terms of administration time. However the PBAC did not accept the re-submission's calculation that there would be a saving in treatment costs based on a 1,000mg dose.

The PBAC considered that there is a clinical need for FCM in Australia as the shorter injection time is likely to provide an advantage for many groups of people who require iron treatment.

The PBAC agreed with the pre-PBAC response that the extent of any change in the setting where iron is infused is subject to a range of factors. These factors include hospital funding models, willingness and ability of general practitioners and specialists to administer IV iron in their rooms and referral practices of medical practitioners. All of these factors are likely to vary significantly between different States, Territories and health care settings.

The PBAC noted that the main driver for the price difference requested was the reduction in public hospital admitted patients. The re-submission claimed that currently 46.13% of patients are admitted as in-patients for iron infusions and 10.82% non-admitted (day only) patients. The PBAC considered that the survey data provided in the re-submission over-estimated the proportion of admitted patients and underestimated the non-admitted patients. In addition the PBAC considered that the proposed changes in private hospitals were unlikely to occur owing to the business models currently in place.

The PBAC agreed with the DUSC that the survey had a number of internal and external validity issues and considered that the extent of switching to community based GP settings could be inflated in the survey.

The PBAC also noted the ESC and DUSC concerns regarding the possible use in haemodialysis patients, where there is no administrative cost advantage and that there was potential for the 500mg vial to be used for lower doses.

The PBAC noted that the sponsor reduced the cost of the 500mg vial to address the potential use of doses greater than 1000mg however the PBAC noted that the pre-PBAC response did not address the potential use in patients requiring smaller doses than 500mg.

Therefore the PBAC considered that the dispensed price for maximum quantity (DMPQ) proposed in the pre-PBAC response was poorly justified and that the expected price advantage for FCM compared to IP would be lower.

On the basis of the costing model in the submission, the PBAC requested the department to calculate a cost-minimised price using the revised treatment setting proportions. The PBAC recommended that the price should take account of the variability in proportions of inpatient and outpatient administration as well as the variability in administration of iron in GP settings.

The PBAC considered that the Department should negotiate a risk sharing arrangement with the sponsor to mitigate the risk of wastage and the potential for larger market uptake in patients treated in health settings with little or no administration benefit. The PBAC did not consider an Authority required listing would be justified for the purposes of a risk sharing arrangement.

The PBAC noted and welcomed the input received from individuals (1) and health care professionals (5) via the Consumer Comments facility on the PBS website. The comments described a range of benefits of treatment with ferric carboxymaltose including reduced infusion time, greater convenience, use of fewer hospital resources, fewer side effects and improved quality of life.

The PBAC considered that ferric carboxymaltose is suitable for inclusion in the list of medicines for prescribing by nurse practitioners within collaborative arrangements.

In accordance with subsection 101 3BA of the National Health Act 1953, the PBAC advised the Minister that it is of the opinion that, on the basis of the material available to it at its November 2013 meeting, ferric carboxymaltose should not be treated as interchangeable on an individual patient basis with any other drug or medicinal preparation.

Outcome:
Recommended

Name, Restriction, Manner of administration and form	Max. Qty	№.of Rpts	Proprietary Name and Manufacturer
FERRIC CARBOXYMALTOSE			
Injection 500mg (iron) in10mL	2	1	Ferinject Vifor Pharma Pty Ltd

Condition/Indication:	Iron deficiency anaemia
Restriction:	Unrestricted

13. Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised in Australia. It considers submissions in this context. A PBAC decision not to recommend listing or not to recommend changing a listing does not represent a final PBAC view about the merits of the medicine. A company can resubmit to the PBAC or seek independent review of the PBAC decision.

14. Sponsor's Comment

Vifor Pharma continues to work with the PBAC to ensure the PBS listing of ferric carboxymaltose for patients with iron deficiency anaemia.